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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/641,081	08/16/2000	Carsten Rosenow	3334.1	3725

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EXAMINER

ZHOU, SHUBO

ART UNIT PAPER NUMBER

1631

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary**Application No.**

09/641,081

Applicant(s)

ROSENOW ET AL.

Examiner

Shubo "Joe" Zhou

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 April 2004 and 15 January 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 January 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendments and request for reconsideration, filed on 1/15/04 and 4/1/04 are acknowledged and the amendments entered. Claims 1-9 are pending and under consideration.
2. The objection to the specification in the previous Office action is hereby withdrawn in view of applicants' amendment to the title and the drawings.
3. The rejection of claims 1-9 under 35 USC 112, second paragraph as being indefinite for containing the limitation of "potentially transcribed" in the claims is hereby withdrawn in view of applicants amendment to the claims.
4. The rejection of claim 1-3 under 35 USC 102(a) as being anticipated by Leary et al. is hereby withdrawn in view of applicants' argument (page 6 of the amendment paper filed 1/15/04).

Drawings

5. The drawing submitted 1/15/04 is acknowledged and accepted.

Claim Rejections-35 USC § 112

6. The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 6-9 are rejected under 35 U.S.C. 112 , second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase “said sub-regions” in claim 6 has no antecedent basis and the claim is thus indefinite. This rejection is reiterated from the previous Office action and maintained for reasons of record. Applicants’ argument filed 1/15/04 has been fully considered but not deemed to be persuasive. Applicants argue that the term “a sub-region” is recited in the preamble and thus “said sub-regions” has antecedent basis. This is not persuasive because the preamble only recites a singular sub-region “a sub-region”, whereas the limitation “said sub-regions” is drawn to plurality of sub-regions.

8. Clarification of the metes and bounds of the phrases are required.

Claim Rejections-35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leary et al. (WO 99/67422, 29 December 1999) in view of Lockhart et al. (US Patent No. 6,040,138, Date of Patent: Mar 21, 2000, filing date: Sep. 15, 1995).

The claims are drawn to a method of identifying a transcribed region in a genome comprising hybridizing probes to transcripts from a genome and identifying a transcribed region if the hybridization signal between a probe and a transcript is above a threshold value.

Leary et al. disclose a method for mapping the position of individual transcript from a genome comprising hybridizing a plurality of nucleic acid probes with a nucleic acid sample wherein the sample comprises transcripts from the genome and the probes are from an area of the genome (page 4, first paragraph) and such probes are immobilized to a substrate (pages 7-8, the bridging paragraph). Leary et al. also disclose that the probes of the genomic fragments can be singled stranded or double stranded (page 9, lines 6-9) and can be oligonucleotides of 20 or more bases (page 9, last paragraph). Leary et al. do not explicitly recite a threshold for the hybridization signal of a region, above which threshold value, the region would be considered as transcribed.

Lockhart et al. teach a method of monitoring gene expression by hybridization of transcripts to high density oligonucleotide arrays. The method comprises hybridizing test transcripts to genomic probes immobilized onto substrates (column 2, Summary of the invention). To reduce the signal/noise ratio, Lockhart et al. teach using different control probes including normalization controls, expression level controls and mismatch control (column 15, line 63 to column 17, line 27). In evaluating the hybridization signals, Lockhart et al. use a different threshold of a test signal above each of the control probe signal for different transcripts

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depending on the expression level of the transcripts in the sample. See column 23, lines 41 to column 24, line 6.

A person of ordinary skill in the art would have been motivated by Lockhart et al. to modify Leary et al. to include the control probes and to use different thresholds for different messages to take advantage of reducing the signal/noise ratios.

In regard to claims 8-9, Leary et al. and Lockhart et al. do not explicitly recite testing a genome of *E. coli* and the transcribed region is an operon, as required in the claims.

However, Leary et al. state that the preferred embodiments in their method include using genomic fragments of bacterial species, most particularly a human pathogen such as *Streptococcus* (page 10, last paragraph). It would have been obvious to a person of ordinary skill in the art that *E. coli* would have been a well-known bacterial pathogen, and the person of ordinary skill in the art would have been motivated to modify Lockhart et al. to include more pathogens including *E. coli*. Further, since it would have been well known to a person of ordinary skill in the art that an operon is part of the *E. coli* genome, which is often transcribed in the presence or absence of certain factors such as inducers or suppressor. Thus, one of ordinary skill in the art would have been motivated to include operon probes in a particular hybridization test to determine whether the operon is transcribed in this particular genome under a particular condition.

This rejection is reiterated from the previous Office action.

Applicant's arguments filed 1/15/04 have been fully considered but they are not persuasive. Applicants' argument is on the ground that the references do not teach setting a threshold for determining a signal to be considered as representing a transcribed region. This is not deemed persuasive because Lockhart et al. clearly teach setting different thresholds of signals (test hybridization intensity/control hybridization intensity) for messages of different expression level. Applicants further argue that there is motivation to combine the references. This is also

non-persuasive because, as set forth above, a person of ordinary skill in the art would have been motivated by Lockhart et al. to modify Leary et al. to use different control probes to reduce the signal/noise ratio, and to take advantage of using different thresholds for messages with different expression levels to not only monitor the expression of genes with high expression level, but also those with low expression level.

Conclusion

12. No claim is allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael

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Woodward, Ph.D., can be reached on 571-272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst William Phillips whose telephone number is 571-272-0548, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

15. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, or on the IFW system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shubo (Joe) Zhou, Ph.D.



Patent Examiner

 14 June 2004
JOHN S. BRUSCA, PH.D.
PRIMARY EXAMINER